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SUBJECT: Application #955

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"Agents which alter the transport, storage and distribution of nicotine".

This study is directed toward investigation of agents that inhibit the transport-mediated uptake of nicotine or its cellular binding, and the events affecting the "translocation" or release of biogenic amines by nicotine. The method used is determination of the concentration of appropriate radio-labeled substances in brain slices exposed to concentrations of the agents to be investigated. Stress will be placed on inhibitors such as procaine and mecamylamine, and the effects of nicotine analogs and antagonists. Comparison of effects in the central nervous system with those in the periphery, such as voluntary or smooth muscle preparations, will be made. A second major effort will be on the interaction between nicotine and biogenic amines, where existing evidence suggests that nicotine alters the distribution of these substances.

## CRITIQUE:

Drs. Weiss and Goodman have already had extensive experience in the use of the proposed method. This has the advantage of providing quantifiable results, but the test system is extracorporeal and thus artificial. The technique is capable of providing only very roughly focused results in terms of localization that might be achievable by the autoradiographic and histochemical methods now readily available. While the budget is modest, this work does not give promise of producing any specially knowledgeable results or concepts.

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